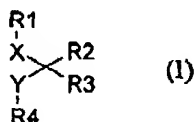


New Title
Please amend the application as follows:

el 13
per amle
In the claims:

This listing of claims will replace all prior versions, and listings, of the claims in the application.

el 16
susceptible to
off much
1. (currently amended) A compound of general Formula I



or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt,

wherein:

OK as per P. 1/14/04
still includes virtually all Hets
all good
 R_1 is selected from the group consisting of:

C_1 - C_6 , C_2 - C_6 alkyl, substituted with one or more basic groups; cycloalkyl, substituted with one or more basic groups; heterocyclyl, comprising at least one nitrogen atom; heterocyclyl, comprising at least one hetero atom selected from S or O, and substituted with one or more basic groups; and aryl, substituted with one or more basic groups;

R_2 is selected from the group consisting of H, acyl, acylamino, alkyl, alkylcarbamoyl, alkylthio, alkoxy, aroyl, aroylamino, aryloxy, arylthio, amidino, amino, aryl, carbamoyl, carboxy, cyano, cycloalkyl, formyl, guanidino, halogen, heterocyclyl, hydroxy, oxo, nitro, thiol, $Z_2N-CO-O-$, $ZO-CO-NZ-$, and $Z_2N-CO-NZ-$;

R_3 is selected from the group consisting of $COOR_5$, $SO(OR_5)$, SO_3R_5 , $P=O(OR_5)_2$, $B(OR_5)_2$, $P=OR_5(OR_5)$, tetrazole, and a carboxylic acid isostere;

R_4 represents a $\begin{array}{c} O-R_5 \\ | \\ P-R_6 \\ | \\ O \end{array}$ -group, or a $\begin{array}{c} O \\ || \\ C-NH \\ | \\ R_7 \end{array}$ -group, or a $\begin{array}{c} O \\ || \\ C-O-R_5 \end{array}$ -group,

R₅ is H, C₁-C₆ alkyl, or aryl;

R₆ is C₁-C₆ alkyl, aryl, cycloalkyl, heterocyclyl, or an optionally N-substituted

H₂N-C(Z)-CONH-C(Z)- or H₂N-C(Z)- group;

R₇ is H or C₁-C₆ alkyl;

X is selected from the group consisting of O, S, SO, SO₂, C(Z)₂, N(Z), NR₇SO₂, SO₂NR₇, NR₇CO, and CONR₇;

Y is selected from the group consisting of O, N(Z), S, C(Z)₂, and a single bond; and

Z is independently selected from the group consisting of H, C₁-C₆ alkyl, aryl, cycloalkyl, and heterocyclyl,

with the proviso that when X is O, S, SO, SO₂, N(Z), NR₇SO₂, SO₂NR₇, or NR₇CO, then Y is C(Z)₂ or a single bond.

2. (previously presented) The compound according to claim 1, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt,

wherein:

R₁ is selected from the group consisting of:

cycloalkyl, substituted with one or more basic groups ;

heterocyclyl, comprising at least one nitrogen atom; and

heterocyclyl, comprising at least one hetero atom selected from S or O, and substituted with one or more basic groups;

R₂ is selected from the group consisting of H, C₁-C₃ alkyl, amino, halogen, and hydroxy;

R₃ is COOR₅;

R_4 represents a $\begin{array}{c} \text{O}-R_5 \\ | \\ -\text{P}-R_6 \\ || \\ \text{O} \end{array}$ -group,

R_5 is H, C_1-C_6 alkyl, or aryl;

R_6 is C_1-C_6 alkyl, aryl, cycloalkyl, heterocyclyl, or an optionally N-substituted

$H_2N-C(Z)-CONH-C(Z)-$ or $H_2N-C(Z)-$ group;

X is $C(Z)_2$;

Y is O or $C(Z)_2$; and

Z is independently H or C_1-C_6 alkyl.

3. (previously presented) The compound according to claim 1, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt,

wherein:

R_1 is selected from the group consisting of:

cycloalkyl, substituted with one or more basic groups;

heterocyclyl, comprising at least one nitrogen atom; and

heterocyclyl, comprising at least one hetero atom selected from S or O, and substituted with one or more basic groups;

R_2 is selected from the group consisting of H, C_1-C_3 alkyl, amino, halogen, and hydroxy;

R_3 is $COOR_5$;

R_4 represents a $\begin{array}{c} \text{O} \\ || \\ \text{C} \\ | \\ \text{N}-\text{OH} \\ | \\ R_7 \end{array}$ -group,

R_5 is H, C_1-C_6 alkyl, or aryl;

R_7 is H or C_1-C_6 alkyl;

X is $C(Z)_2$;

Y is C(Z)₂ or a single bond; and
Z is independently H or C₁-C₆ alkyl.

4. (previously presented) The compound according to claim 1, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt,

wherein

R₁ is selected from the group consisting of:

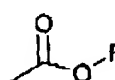
cycloalkyl, substituted with one or more basic groups;

heterocyclyl, comprising at least one nitrogen atom; and

heterocyclyl, comprising at least one hetero atom selected from S or O, and substituted with one or more basic groups;

R₂ is selected from the group consisting of H, C₁-C₃ alkyl, amino, halogen, and hydroxy;

R₃ is COOR₅;

R₄ is a -R₅-group;


R₅ is H, C₁-C₆ alkyl, or aryl;

X is C(Z)₂;

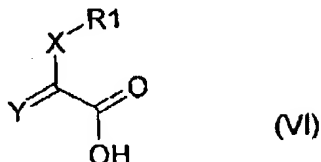
Y is C(Z)₂ or a single bond; and

Z is independently H or C₁-C₆ alkyl.

5. (previously presented) A process for the preparation of a compound according to any one of claims 1-4, wherein R₁, R₅, R₆, and Z are as defined in claim 1, R₂ is H, R₃ is COOR₅,

R₄ represents a -group.

X is C(Z)₂, and Y is C(Z)₂,
comprising the step of:
reacting a compound of Formula VI,

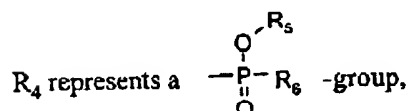


wherein R₁ and Z is as defined in claim 1, X is C(Z)₂, and Y is C(Z)₂, with a compound of Formula IX,

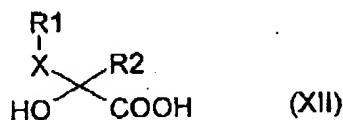


wherein R₆ is as defined in claim 1, in the presence of a reagent, under standard conditions.

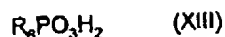
6. (previously presented) A process for the preparation of a compound according to any one of claims 1-4, wherein R₁, R₂, R₅, R₆, and Z are as defined in claim 1, R₃ is COOR₅, X is C(Z)₂, Y is O, and



comprising the step of:
reacting a compound of Formula XII,



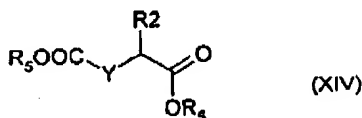
wherein R_1 and R_2 are as defined in claim 1 and X is $C(Z)_2$, with a compound of Formula XIII,



wherein R_6 is as defined in claim 1, in the presence of a coupling reagent under standard conditions.

7. (currently amended) A process for the preparation of a compound according to any one of claims 1-4,

wherein R_1 and R_2 are as defined in claim 1, X is $C(Z)_2$, and Y is are independently $C(Z)_2$ or a single bond, and R_3 and R_4 are $COOR_5$, comprising the step of:
reacting a compound of Formula XIV,

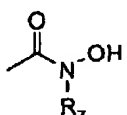


wherein R_2 and R_5 are as defined in claim 1, and Y is $C(Z)_2$ or a single bond, with a compound of the general Formula III,

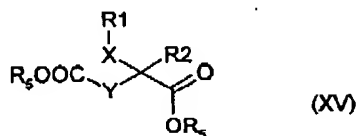


wherein R_1 is as defined in claim 1, X is $C(Z)_2$, and L is a leaving group, in the presence of a base, under standard conditions.

8. (previously presented) A process for the preparation of a compound according to any one of claims 1-4, wherein R_1 , R_2 , R_5 , R_7 , X, Y and Z are as defined in claim 1, R_3 is COOR_5 and

R_4 represents a -group,

comprising the step of:
reacting a compound of Formula XV,



with a compound of Formula XVI,



wherein R_7 is as defined in claim 1, in the presence of a reagent under standard conditions.

9. (previously presented) A pharmaceutical formulation comprising a compound according to any one of claims 1-4 as active ingredient in combination with a pharmaceutically acceptable adjuvant, diluent, or carrier.

10. (cancelled)

11. (cancelled)

12. (previously presented) A method for the treatment or prophylaxis of conditions associated with inhibition of carboxypeptidase U, comprising administering to a patient in need of such treatment an effective amount of a compound according to any one of claims 1-4.

13. (previously presented) A pharmaceutical formulation for the treatment or prophylaxis of conditions associated with inhibition of carboxypeptidase U, comprising a compound according to any one of claims 1-4 in combination with a pharmaceutically acceptable adjuvant, diluent, or carrier.

14. (previously presented) A pharmaceutical formulation, comprising:

- (i) a compound of Formula I as defined in claim 1 or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt; and
 - (ii) one or more antithrombotic agents with a different mechanism of action from that of component (i),
- in admixture with a pharmaceutically acceptable adjuvant, diluent, or carrier.

15. (previously presented) A kit of parts comprising:

- (i) a pharmaceutical formulation comprising a compound of Formula I as defined in claim 1, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier; and
- (ii) a pharmaceutical formulation comprising one or more antithrombotic agents with a different mechanism of action from

that of component (i), in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier;
wherein compound (i) and agent (ii) are each formulated for administration in conjunction with the other.

16. (previously presented) A method for treatment of a patient suffering from, or susceptible to, a condition in which inhibition of carboxypeptidase U and a different antithrombotic mechanism are required or desired, which method comprises administering to the patient a therapeutically effective total amount of:

- (i) a compound of Formula I, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier; and
- (ii) one or more antithrombotic agents with a different mechanism of action from that of component (i), in admixture with a pharmaceutically acceptable adjuvant, diluent, or carrier.

17. (previously presented) A method for treatment of a patient suffering from, or susceptible to, a condition in which inhibition of carboxypeptidase U and a different antithrombotic mechanism are required or desired, which method comprises administering to the patient a formulation from the kit of claim 15.

18. (previously presented) The compound according to any one of claims 1-4, wherein the basic group is selected from the group consisting of amino, amidino, and guanidino.

19. (previously presented) The process according to claim 5, wherein the reagent is N,O-bis(trimethylsilyl)acetamide (BSA) or hexamethyldisilazane (HMDS).
20. (previously presented) The process according to claim 6, wherein the coupling reagent is selected from the group consisting of:
 - (i) dicyclohexylcarbodiimide (DCC)/N,N-dimethyl amino pyridine (DMAP);
 - (ii) (benzotriazol-1-yloxy)tripyrrolidinophosphonium hexafluorophosphate (PyBop)/ diisopropylethylamine (DIPEA); and
 - (iii) SOCl₂.
21. (previously presented) The process according to claim 7, wherein the leaving group is selected from the group consisting of Cl, Br, I, and tosyl.
22. (previously presented) The process according to claim 7, wherein the base is lithium diisopropylamide (LDA) or NaH.
23. (previously presented) The process according to claim 8, wherein the reagent is dicyclohexylcarbodiimide (DCC)/N,N-dimethyl amino pyridine (DMAP).
24. (previously presented) The formulation according to claim 14, wherein the antithrombotic agent with a different mechanism of action is selected from the group consisting of an antiplatelet agent, thromboxane receptor inhibitor, synthetase inhibitor, fibrinogen receptor antagonist, prostacyclin mimetic, phosphodiesterase inhibitor, and an ADP-receptor (P₂T) antagonist.

25. (previously presented) The kit according to claim 15, wherein the antithrombotic agent with a different mechanism of action is selected from the group consisting of an antiplatelet agent, thromboxane receptor inhibitor, synthetase inhibitor, fibrinogen receptor antagonist, prostacyclin mimetic, phosphodiesterase inhibitor, and an ADP-receptor (P_2T) antagonist.

26. (previously presented) The method according to claim 16, wherein the antithrombotic agent with a different mechanism of action is selected from the group consisting of an antiplatelet agent, thromboxane receptor inhibitor, synthetase inhibitor, fibrinogen receptor antagonist, prostacyclin mimetic, phosphodiesterase inhibitor, and an ADP-receptor (P_2T) antagonist.